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Rate of decline of antibody titres to influenza A/California/7/2009 (H1N1) by haemagglutination inhibition and virus neutralization assays in a cohort of seroconverting adults in Singapore

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Background: The rate of decline of antibody titres to influenza following infection can affect results from sero-surveys, and population level decline in such titres may explain the pattern of repeat epidemics observed in pdmH1N1 influenza A. We describe changes in antibody titres in a cohort of adults who seroconverted during the initial wave of pdmH1N1 infections in Singapore.

Methods: We followed up a cohort who seroconverted (≥4-fold increase in haemagglutination inhibition (HI) titres to A/California/7/2009 H1N1) during a sero-incidence study in 2009 and obtained 2 additional blood samples in April 2010 and September 2010, which were assayed for antibodies to A/California/7/2009 H1N1 by both HI and virus microneutralization (MN) assays along with the sample from 2009 with the highest HI titres (between August and Oct 2009). We analysed pair-wise mean-fold change in titres and the proportion with HI titres ≥40 at the three time points; for MN, a cut-off point of ≥160 was used as this best correlated with a HI titre of 40 in our assays (Figure 1).

Results: 67 participants contributed 3 samples each. From the 2009 sample to the last sample in 2010, 2 participants had an increase in titres (on both HI and MN), while 63 (94%) and 49 (73%) had a decrease in HI and MN titres respectively. Titres by both assays decreased significantly; the mean-fold decrease was 2.0 by HI and 4.9 by MN (Figure 2). While 70% and 72% had titres ≥40 and ≥160 by HI and MN in 2009, this decreased to 21% and 37% by September 2010. In 6 individuals aged 55 and older, the mean-fold decrease was 11.3 compared to 4.5 in those aged below 55 years by HI (p=0.035), and 4.5 vs 1.9 by MN (p=0.021).

Conclusion: After 1 year, only 21% individuals with serologically ascertained pdmH1N1 infection had the traditionally accepted sero-protective HI titres of ≥40. The drop in titres was more marked by HI than MN, with implications for serological studies. The significance for re-infection is uncertain but the rapid decline may explain the multiple infection waves observed. There was also evidence that titres decreased more rapidly in older individuals.

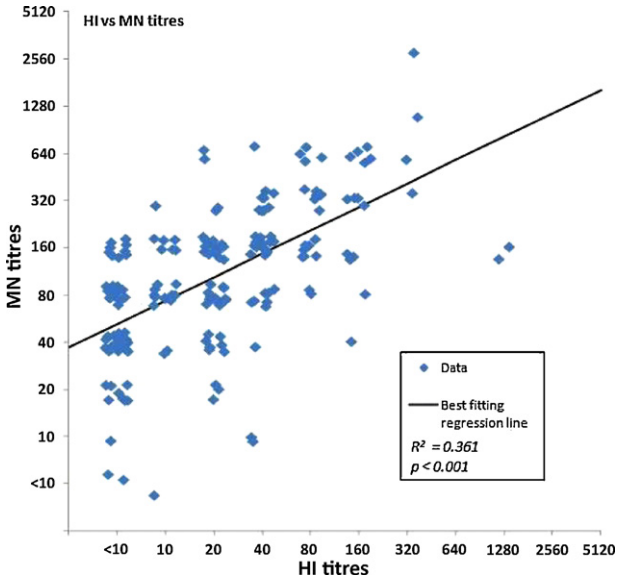

Figure 1. Pairs of HI vs MN titres for all 201 samples. Note that random jitter has been used to separate overlapping data points.

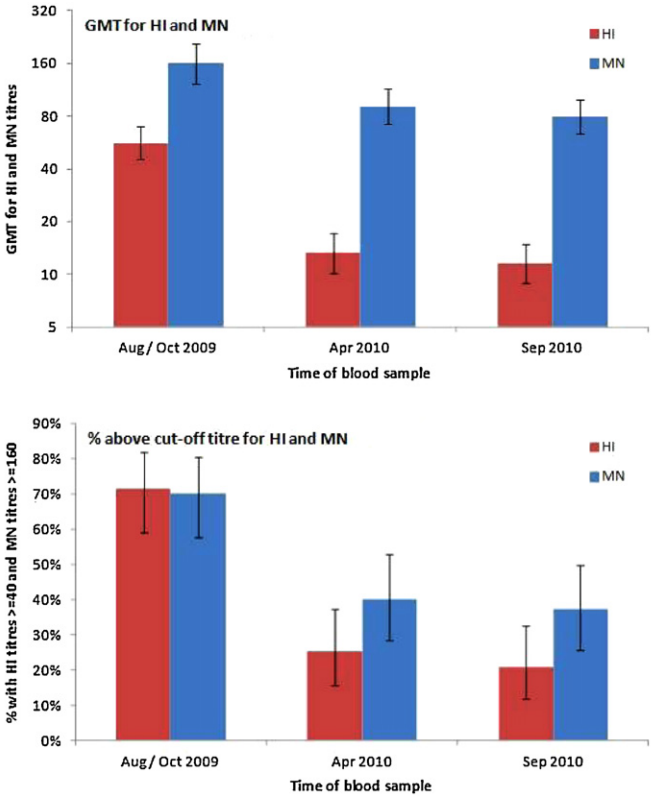

Figure 2. Changes in titres over time by HI and MN assays. A) GMT B) % with titres >=40 by HI and >=160 by MN.

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Clinical presentation and health-seeking behaviour for acute respiratory illness episodes in a cohort of community dwelling adults during the initial wave of pdmH1N1 influenza A from June to September 2009 in Singapore

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Background: For pdmH1N1 influenza, presentation to medical care was an entry point for interventions like antiviral treatment, and influenza-like illness (ILI) reporting by care providers was also